--84. A method for quantitative structure function analysis research on biologically active proteins or peptides, said method comprising applying a specific chemical modification of selected amino acids to introduce at least one feature selected from the group consisting of enhanced biological activity, enhanced stability, suppressed antigenicity, acquired antagonistic activity, and cell inhibitory activity is introduced into said proteins or peptides, said method comprising the steps of

a) gradual chemical modification of a protein or peptide, followed by

b) monitoring the modification reaction with a mild and sensitive method such as nondenaturing electrophoresis or electrospray mass spectrometry and optionally confirming the overall structural integrity;

c) protease treatment;

d) mass spectrometry;

e) assaying biological activity of the modified product and optionally assaying stability of the modified product.

85. The method according to claim 84 wherein said proteins or peptides are selected from the group consisting of interleukins, haemopoietic growth factors, peptide hormones, protein hormones, signal peptides and signal proteins.

86. The method according to claim 84 wherein said protein or peptide is selected from the group consisting of the cytokine superfamily, insulin, and prolactin.

87. The method according to claim 86 wherein said protein or peptide is a member of the cytokine superfamily selected from the group consisting of interleukins 1-8, interleukin 10, CM-CSF, TNF, gamma IFN and EPO.

88. The method according to claim 87 wherein said protein or peptide is an interleukin selected from interleukins 1-7.

B' cont

89. The method according to claim 56 wherein said endoprotease is Endo Glu C or Endo Lys C.

90. The method of claim 57 wherein the exoprotease is Cathepsine C or carboxypeptidase Y.

91. The substance according to claim 73 which is human interleukin 3 which has been modified at one or more of the following residues: Ala^{1}, His^{26}, Lys^{28}, Lys^{66}, His^{95}, His^{98}, Lys^{100}, or Lys^{116}.

92. A preparation for clinical application comprising a substance according to one of claims 66-68 and an additional signal protein or peptide.--

Amend the remaining claims as follows:

In claim 55, on line 1, change "1" to --84--.

56. (Amended) A method according to claim [1 or 2] 84 or 55 wherein specific digestion with specific endoproteases and LDMS is carried out for characterisation and localisation of the modified amino acids[, said endoprotease for example being Endo Glu C or Endo Lys C.]

57. (Amended) A method according to [any of claims 1-3] claim 84 or 55 wherein the modification is carried out by specific digestion with specific exoproteases and electrospray mass spectrometry is carried out for characterisation and localisation of the modified amino acids[, suitably the exoprotease is N terminal e.g. Cathepsine C or C terminal e.g. carboxypeptidase Y].

In claim 58, on line 1, change "any of claims 1-3" to --claim 84 or 55--.

In claim 59, on line 1, change "5" to --58--.

60. (Amended) A method according to [one or more of the preceeding claims] claim 84 or 55 for the introduction of an antagonistic [and/or] or cell inhibitory activity, wherein the modification has specificity to one or more residues that are involved in catalytic activity [e.g. where the modification is within or in close proximity to a partial or complete catalytic center, said modification preferably changing the catalytic activity, suitably said residue is a histidine residue].

B3

In each of claims 61, 62, 63, 64 and 65, on line 1, change "one or more of the preceeding claims" to --claim 84 or 55--.

66. (Amended) A modified signal substance[, preferably] selected from the group consisting of a protein hormone, peptide hormone, growth factor, a haemopoeitic growth factor, an interferon, an interleukin [and/or] and a colony stimulating factor with enhanced biological activity, antagonistic activity [and/or] or cell inhibitory activity, wherein [the] said signal substance contains a modification [is] within or in close proximity to a [partial or complete] catalytic center, preferably such that the catalytic activity is changed, said modification further preferably being within or in close proximity to a metal binding center.

B4

In claim 68, line 1, change "14" to --67--.

69. (Amended) A substance[, as described in one or more of the preceding substance claims 13-15,] according to one of claims 66-68, wherein the modification for producing an antagonist is a chemical modification, preferably an alkylation, an acylation or molecular biological modification like a deletion mutation and/or a substitution mutation[, preferably the modification is an alkylation].

70. (Amended) A substance[, as described in one or more of the preceding substance claims 13-16,] according to one of claims 66-68 wherein the modification is of an amino acid involved in the binding of a metal ion[, preferably a Histidine residue].

B5

71. (Amended) A substance[, as described in one or more of the preceding substance claims 13-17,] according to one of claims 66-68 wherein the affinity of the signal substance for the receptor has not decreased by more than a factor of 10[, preferably has remained the same and more preferably has increased].

72. (Amended) A substance according to [any of the preceding substance claims 13-18,] according to one of claims 66-68 wherein the concentration of substance required for

significant inhibition is suitable for clinical application, being [i.e.] less than a hundred fold higher than the native substance concentration, said substance optionally further having increased receptor binding capacity.

B5 cont

73. (Amended) A substance according to [any of the preceding substance claims, 13-19] according to one of claims 66-68 wherein the substance is interleukin 3 [preferably human interleukin 3, most preferably modified only at one or more of the following residues: Ala^{1}, His^{26}, Lys^{28}, Lys^{66}, His^{95}, His^{98}, Lys^{100}, or Lys^{116}].

In claim 74, on line 1, change "20" to --73--.

In claim 75, on lines 1-2, delete "as described in... claims 13-21," and insert therefor --according to one of claims 66-68--.

In claim 78, on line 1, change "inhibition, suppression and/or cure" to --obtaining at least inhibition or suppression--.

In claim 80, line 1, delete "25 or 26" and insert therefor --78--.

In claim 81, line 1, delete "the preceding method claims 25-27" and insert therefor --claims 78 and 80--.

In claim 83, line 2, change "13-22" to --66-68--.